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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,753	10/09/2001	Alan J. Schroit	UTSC:594USD1/MBW	8205

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EXAMINER	
NICKOL, GARY B	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,753	SCHROIT, ALAN J.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response filed on January 9, 2003 (Paper No. 6) to the restriction requirement of December 16, 2002 has been received. Applicant has elected Group III, claims 10-11 for examination without traverse.

Claims 1-27 were cancelled.

Claims 28-36 were added and are currently under examination.

Information Disclosure Statement

The IDS filed 02-08-02 (Paper No. 4) has been considered, in part. However, some of the references (see those lined through) were no longer available from applicant's earlier application (09/224558). The Examiner apologizes for any inconvenience on the part of the Office.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 30-36, as written, do not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended

to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 17 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28, 30, and 33-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making an antibody that specifically binds to phosphatidylserine comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylserine/polypeptide conjugate, does not reasonably provide enablement for an anti-phosphatidylserine antibody or method of making said antibody by administrating a **phosphatidylcholine**/polypeptide conjugate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to antibodies, including monoclonal, that specifically binds to phosphatidylserine (PS); a method of making an antibody that specifically binds to phosphatidylserine comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylserine/polypeptide conjugate or a phosphatidylcholine/polypeptide conjugate.

The claims are not enabled because there is insufficient guidance and objective evidence to predictably enable one of skill in the art to isolate and or make specific antibodies to PS (including monoclonal antibodies) comprising administering a **phosphatidylcholine (PC)**/polypeptide conjugate.

Although the specification teaches (page 38) that antisera from rabbits immunized against PS-BSA conjugates reacted with PS and DOPE, the specification does not teach the specificity of antisera from rabbits immunized against a PC/polypeptide conjugate. Furthermore, PS and PC differ distinctly in their molecular composition and charge. For example, the head-group serine has a different number of carbon and oxygens atoms from the head group choline. Also, PS has a net charge of –1 (at neutral pH) while PC has a neutral charge. These differences in molecular architecture and charge, compounded by the lack of guidance in the specification, make it unpredictable that animals immunized with a PC/polypeptide conjugate would predictably generate antibodies that react specifically with a different phospholipid, such as PS. Furthermore, it is highly unpredictable that a monoclonal antibody specific for PS could be made from immunizing animals with PC/polypeptide conjugates because of these differences in charge and molecular structure.

Thus, based on the above, it would require undue experimentation to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Umeda *et al.* (Jnl. of Immunology, Vol. 143, No. 7, pages 2273-2279, IDS)

Umeda *et al.* teach monoclonal antibodies that specifically bind to phosphatidylserine (see abstract). Umeda *et al.* further teach the linkage of the antibodies to detectable labels wherein the antibody is linked to biotinylated rabbit anti-mouse immunoglobulins and peroxidase conjugated streptavidin (page 2274, materials & methods); all of which read on detectable labels comprising biotin and hydrogen peroxidase.

Although the prior art does not specifically teach wherein said antibody is "made by a process comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of phosphatidylcholine/polypeptide or a phosphatidylserine/polypeptide conjugate composition" or "wherein a composition comprising phosphatidylserine/BSA, phosphatidylserine/KLH, phosphatidylserine/BGG, or phosphatidylserine/β2-glycoprotein I conjugate is administered to the animal" (Claim 31) or

wherein said "polypeptide is β2-glycoprotein I" (Claim 32), the claims read solely on the product *per se*, an antibody that specifically binds to phosphatidylserine. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claims 28-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Bate *et al.* (Immunology, Vol. 79, 1993, pages 138-145, IDS).

Bate *et al.* teach a method of making an antibody that specifically binds to phosphatidylserine comprising administering to an animal a pharmaceutical composition comprising an immunologically effective amount of a phosphatidylserine/polypeptide conjugate wherein a composition comprising phosphatidylserine/KLH (PS-KLH) conjugate is administered to the animal (abstract). Hence, such antisera contains an antibody that specifically binds to phosphatidylserine wherein Bate *et al.* teach (page 144, 2nd paragraph) that PS-KLH gave rise to the most specific antibodies judging by the results of adsorption experiments with the different sorts of liposomes.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
March 18, 2003